Dechert LLP

FAX TRANSMISSION SHEET

DATE: April 15, 2003

TO:	Examiner Liu, Hong	FAX: 703.746.5122	TEL: 703.306.5814
CC:		FAX:	TEL:
FROM:	Arthur E. Jackson, Ph.D.	FAX: 609.620.3259	TEL: 609.620.3254
ROOM:		EMAIL: Arthur.Jackson@dechert.com	
CLIENT:	361331-512	MATTER: 301200	

TOTAL PAGES (INCLUDING COVER SHEET): 6

BOSTON
BRUSSELS
FRANKFURT
HARRISBURG
HARTFORD
LONDON
LUXEMBOURG
NEW YORK
NEWPORT BEACH
PARIS
PHILADELPHIA
PRINCETON
SAN FRANCISCO
WASHINGTON

MESSAGE

Re: 10/036,857

Elected Compounds

149571.1.07

IF ALL PAGES ARE NOT RECEIVED, PLEASE CALL 609.620.3204

Law Offices of Dechert LLP
A Pennsylvania Limited Liability Partnership — James J. Marino • Resident Managing Partner
Princeton Pik Corporate Center • P.O. Box 5218 • Princeton, NJ 08543-5218
T l: 609.620.3200 • Fax: 609.620.3259 • www.dechert.com
Deliv ry Address: 997 Lenox Dr., Bldg. 3, Ste. 210 • Lawrenceville, NJ 08648

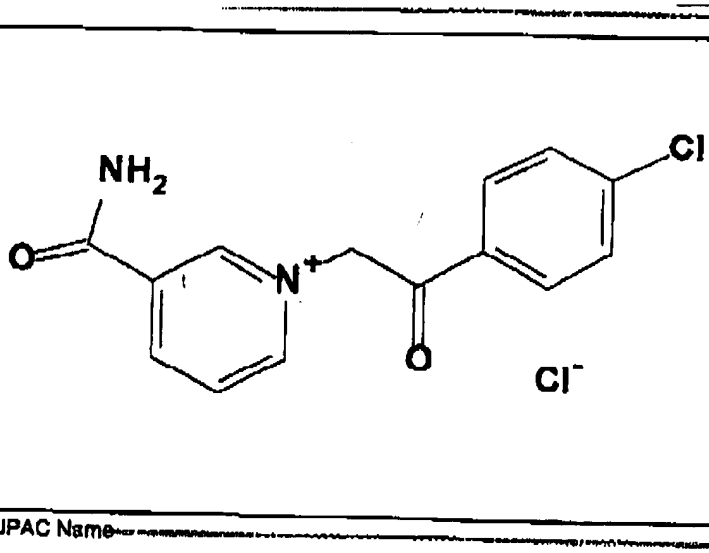
Atherton Ex Liu, Hong

No 10/036,857

703-746-5122 fx

703-306-5814 ph

Elected compound



Formula: $C_{14}H_{12}Cl_2N_2O_2$

Mol Wt: 311.167

CLogP: -1.5154

Chemist: M.Pagan

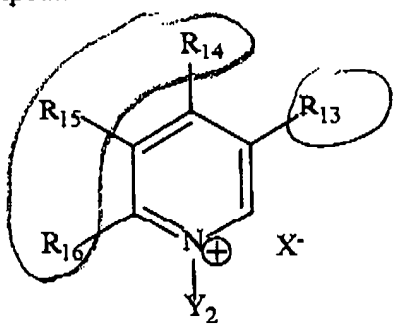
Quantity:

MP: 284-285C

IUPAC Name: 3-Carbamoyl-1-[2-(4-chloro-phenyl)-2-oxo-ethyl]-pyridinium; chloride

Solubility: Alcohols, Water and DMSO

28. A compound of formula VI:



(VII)

wherein

a. R^{13}, R^{14}, R^{15} and R^{16}

1. are independently selected from hydrogen, acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylamino, (C_1-C_3)alkylenedioxy, allyl, amino, ω-alkylenesulfonic acid, carbamoyl, carboxy, carboxyalkyl, cycloalkyl, dialkylamino, halo, hydroxy, (C_2-C_6)hydroxyalkyl, mercapto, nitro, sulfamoyl, sulfonic acid, alkylsulfonyl, alkylsulfinyl, alkylthio, trifluoromethyl, azetidin-1-yl, morpholin-4-yl, thiomorpholin-4-yl, piperidin-1-yl, 4-[C_6 or C_{10}]arylpiperidin-1-yl, 4-[C_6 or C_{10}]arylpiperazin-1-yl, Ar^3 (wherein Ar^3 is C_6 or C_{10} aryl), Ar^3–alkyl, Ar^3-O, Ar^3SO_2-, Ar^3SO-, Ar^3S-, Ar^3SO_2NH-, Ar^3NH, (N-Ar^3)(N-alkyl)N-, $Ar^3C(O)$-, $Ar^3C(O)NH$-, Ar^3NH-C(O)-, and (N-Ar^3)(N-alkyl)N-C(O)-, or together R_1 and R_2 comprise methylenedioxy; or

2. form, with an adjacent pair from R^{13}, R^{14}, R^{15} and R^{16}, together with their ring carbons, a C_6- or C_{10}- aromatic fused ring system; or

3. form, with an adjacent pair from R^{13}, R^{14}, R^{15} and R^{16}, together with their ring carbons, a C_5-C_7 fused cycloalkyl ring having up to two double bonds including the fused double bond of the pyridinium containing ring, which cycloalkyl ring can be substituted by one or more of the group consisting of alkyl, alkoxycarbonyl, amino, aminocarbonyl, carboxy, fluoro, or oxo substituents; or

4. form, with an adjacent pair from R^{13}, R^{14}, R^{15} and R^{16}, together with their ring carbons, a 5- or 6-membered heteroaryl ring, wherein the 6-membered heteroaryl ring contains one to three atoms of N, and the 5-membered heteroaryl ring contains from on to three atoms of N or one atom of O or S and zero to two atoms of N, each heteroaryl ring may be optionally substituted with one or more 1-pyrrolidinyl-, 4-[C_6 or C_{10}]arylpiperazin-1-yl, 4-[C_6 or C_{10}]arylpiperidin-1-yl,

wherein Rs is a [C_6 or C_{10}]aryl or a heterocycle containing 4-10 ring atoms of which 1-3 are heteroatoms selected from the group consisting of oxygen, nitrogen and sulfur; or Rs,

Rs Inadvertently omitted but defined on pp. 4:25-28

azetidin-1-yl, morpholin-4-yl, thiomorpholin-4-yl, piperidin-1-yl, halo or (C_1-C_3)alkylenedioxy groups; or

5. form, with an adjacent pair from R^{13}, R^{14}, R^{15} and R^{16}, together with their ring carbons, a five to eight membered heterocycle, wherein the heterocycle consists of ring atoms selected from the group consisting of carbon, nitrogen, and $S(O)_n$, where n=0,1, or 2;

b. Y^2 is a group of the formula $-CH(R^5)-R^6$ wherein

(a) R^5 is hydrogen, alkyl-, cycloalkyl-, alkenyl-, alkynyl-, aminoalkyl-, dialkylaminoalkyl-, (N-[C_6 or C_{10}]aryl)(N-alkyl)aminoalkyl-, piperidin-1-ylalkyl-, 1-pyrrolidin-1-ylalkyl, azetidinylalkyl, 4-alkylpiperazin-1-ylalkyl, 4-alkylpiperidin-1-ylalkyl, 4-[C_6 or C_{10}]arylpiperazin-1-ylalkyl, 4-[C_6 or C_{10}]arylpiperidin-1-ylalkyl, azetidin-1-ylalkyl, morpholin-4-ylalkyl, thiomorpholin-4-ylalkyl, piperidin-1-ylalkyl, [C_6 or C_{10}]aryl, or independently the same as R^6;

(b) R^6 is phenyl substituted at the para position with chloro or fluoro;

(2) a group of the formula –W–Rs, wherein W is –C(=O)– or $-S(O)_n-$ where n=1 or 2;

(3) a group of the formula $-W-N(R^9)R^{10}$, wherein

[a] R^9 is hydrogen and R^{10} is an alkyl or cycloalkyl, optionally substituted by

(i) [C_6 or C_{10}]aryl, or

(ii) a 5- or 6-membered heteroaryl ring, wherein the 6-membered heteroaryl ring contains one to three atoms of N, and the 5-membered heteroaryl ring contains from one to three atoms of N or one atom of O or S and zero to two atoms of N, said heteroaryl ring can be optionally substituted with one or more 1-pyrrolidinyl, 4-[C_6 or C_{10}]arylpiperazin-1-yl, 4-[C_6 or C_{10}]arylpiperidin-1-yl, azetidin-1-yl, and morpholin-4-yl, thiomorpholin-4-yl, piperidin-1-yl, halo or (C_1-C_3)alkylenedioxy groups, or fused to a phenyl or pyridine ring, wherein the ring fusion is at a carbon-carbon double bond of the heteroaryl ring, or

(iii) a heterocycle containing 4-10 ring atoms of which 1-3 are heteroatoms selected from the group consisting of oxygen, nitrogen and sulfur; or

[b] R^9 is hydrogen or lower alkyl and R^{10} is Ar^3; or

[c] R^9 is hydrogen or lower alkyl, and R^{10} is a heterocycle containing 4-10 ring atoms of which 1-3 are heteroatoms are selected from the group consisting of oxygen, nitrogen and sulfur, said heterocycle; or

[d] R^9 and R^{10} are both alkyl groups; or

[e] R^9 and R^{10} together with N form a heterocycle containing 4-10 ring atoms which can incorporate up to one additional heteroatom selected from the group of N, O or S in the ring, wherein the heterocycle is optionally substituted with (C_6-or C_{10})aryl, (C_6-or C_{10})arylalkyl, or a 5- or 6-membered heteroaryl ring, wherein the 6-membered heteroaryl ring contains one to three atoms of N, and the 5-membered heteroaryl ring contains from one to three atoms of N or one atom of O or S and zero to two atoms of N, each such heteroaryl can be optionally substituted with one or more 1-pyrrolidinyl, 4-[C_6 or C_{10}]arylpiperazin-1-yl, 4-[C_6 or C_{10}]arylpiperidin-1-yl, azetidin-1-yl, morpholin-4-yl, thiomorpholin-4-yl, piperidin-1-yl, halo or (C_1-C_3)alkylenedioxy; or

[f] R^9 and R^{10} are both hydrogen;

c. X is a pharmaceutically acceptable anion, or

(B) a pharmaceutically acceptable salt of the compound,

wherein aryl or Ar^3 can be substituted with, in addition to any substitutions specifically noted, one or more general substituents selected from the group consisting of acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylamino, (C_1-C_3)alkylenedioxy, alkylsulfonyl, alkylsulfinyl, ω-alkylenesulfonic acid, alkylthio, allyl, amino, $Ar^3C(O)$-, $Ar^3C(O)NH$-, Ar^3O-, Ar^3-, Ar^3-alkyl-, carboxy, carboxyalkyl, cycloalkyl, dialkylamino, halo, trifluoromethyl, hydroxy, (C_2-C_6)hydroxyalkyl, mercapto, nitro, sulfamoyl, sulfonic acid, 1-pyrrolidinyl, 4-[C_6 or C_{10}]arylpiperazin-1-yl-, 4-[C_6 or C_{10}]arylpiperidin-1-yl, azetidin-1-yl, morpholin-4-yl, thiomorpholin-4-yl, piperidin-1-yl;

wherein heterocycles, except those of Ar^3, can be substituted with, in addition to any substitutions specifically noted, the following general substitutions: acylamino, alkanoyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylamino, alkylsulfonyl, alkylsulfinyl, alkylthio, amino, $Ar^3C(O)$-, Ar^3O-, Ar^3-, carboxy, dialkylamino, fluoro, fluoroalkyl, difluoroalkyl, hydroxy, mercapto, sulfamoyl, or trifluoromethyl;

wherein, if the compound of formula VII has a core structure comprising a pyridinium ring having a 2-aryl-2-oxoethyl substitution at the 1 position, wherein the aryl can be substituted, and a formyl which may be substituted at the 3 position, one or both of the following applies:

the compound of formula VII differs from a salt of pyridinium compound having a 1-(2-aryl-2-oxoethyl), wherein the aryl can be substituted, and a formyl which may be substituted at the 3 position by at least one additional substitution at R^{14}, R^{15} or R^{16}, or

the aryl of 2-aryl-2-oxoethyl is phenyl and is substituted at the para position with an electron withdrawing group selected from fluoro, chloro, nitro, trifluoromethyl, and carbamoyl; and

wherein the compound of formula VII differs from a salt of 1-[2-(4-methylphenyl)-2-oxoethyl]-pyridinium by one or more of the lack or replacement of the methyl substitution, or the presence of one or more additional substitutions.